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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/708,204	02/16/2004	Itzhak Bentwich	050992.0201.03USCP	2203
37808	7590	08/21/2009		
ROSETTA-GENOMICS c/o POLSINELLI SHUGHART PC 700 W. 47TH STREET SUITE 1000 KANSAS CITY, MO 64112			EXAMINER WOLLENBERGER, LOUIS V	
			ART UNIT 1635	PAPER NUMBER
			MAIL DATE 08/21/2009	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/708,204	Applicant(s) BENTWICH, ITZHAK	
	Examiner Louis Wollenberger	Art Unit 1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 15 May 2009 and 19 May 2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 31, 32 and 39-42 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 31 is/are allowed.
- 6) ☒ Claim(s) 32 and 39-42 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>5/15/2009</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Status of Application/Amendment/Claims

Applicant's response and supplemental response filed 5/15/2009 and 5/19/2009, respectively, including the Declaration under 37 CFR 1.132 by Ayelet Chajut, have been considered. Rejections and/or objections not reiterated from the previous office action mailed 12/15/2008 are hereby withdrawn. The following rejections and/or objections are either newly applied or are reiterated and are the only rejections and/or objections presently applied to the instant application. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Also acknowledged are applicant's amendments to the claims filed 5/15/2009. With entry of the amendment, claims 31, 32, and 39-42 are pending and under examination.

Applicant's amendment to the specification is acknowledged. The amendment has been entered into the application.

Priority

The previous Action acknowledged Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c), and 35 U.S.C. 119(a)-(d).

It was stated Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119(a)-(d), 119(e), and 120 as follows: The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed

application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

It was stated the disclosures of prior-filed Application Nos. 60/468,251, 10/649,653, 10/651,227, 10/707,147 11/24/2003, 10/604,985, 10/604,926, 10/604,727, 10/604,726, 10/707,975, 10/707,980, and PCT/IL03/00998 fail to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for the instant claims drawn to SEQ ID NO:6527 and 15. That is, written description support for SEQ ID NO:6527 and 15 is not readily found in any of the prior filed applications to which priority is now claimed.

In reply, Applicant stated and the Examiner noted instant SEQ ID NO:15 and 6527 are identical to SEQ ID NO:303 and 169, respectively, in Application No. 10/707,147, filed 11/24/2003. In view of Applicant's Remarks, for purposes of this examination the earliest effective filing date of the instant claims continues to be that of 10/707147: 11/24/2003.

The lack of priority finding is maintained, however, with regard each of the other prior-filed applications to which priority is claimed.

Specification

The application contains disclosure entirely outside the bounds of the allowed claims. Applicant is required to modify the brief summary of the invention and restrict the descriptive matter so as to be in harmony with the claims (MPEP § 1302.01).

In the instant case the specification incorporates by reference several large tables, Tables 1-11, submitted to the Office in the form of compact discs, which, altogether, are said by

applicant to contain several thousand kilobytes of information, the large majority of which is not pertinent to the claimed invention: SEQ ID NO:348 and 4233864.

Using the conversion factor set forth in 37 CFR 1.52(f)(1), the electronic information contained in Tables 1-11 represents thousands of sheets of additional disclosure beyond the approximately 153 pages of paper copy specification filed therewith. A review of Tables 1-11 finds the tables disclose information directed to hundreds of thousands of different nucleotide sequences that have no disclosed relation to the claimed sequences.

In addition to the requirement under MPEP 1302.01, Applicant is required under 37 CFR 1.52(e)(5) to amend the specification to include in the paper portion of the specification all descriptive matter pertinent to SEQ ID NO:6527 and 15 that was previously submitted in tables on compact disc. Amendments to the specification must comply with 37 CFR 1.121 and 1.125.

Claim Rejections - 35 USC § 101 and 112, First Paragraph—withdrawn

The rejection of Claims 31, 32, and 39-42 under 35 U.S.C. 101 and 35 USC 112, first paragraph, because the claimed invention is not supported by a credible asserted utility is withdrawn upon further consideration in view of the totality of evidence of record.

Claim Rejections - 35 USC § 103—withdrawn

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

The rejection of Claims 31, 32, and 39-42 under 35 U.S.C. 103(a) as being unpatentable over Venter et al. (US Patent 6,812,339) and Zhao et al. (1997) GenBank Acc. No. AQ420078, first seen at NCBI on Mar 23 1999 12:30 AM, in view of

1. Buck et al. (Biotechniques (1999) 27(3): 526-538);
2. Hogan (US Pat. 5,541,308, July 30, 1996); and
3. Brown (1998) "In situ hybridization with riboprobes: An overview for veterinary pathologists" *Vet. Pathol.* 35:159-167

is withdrawn in view upon further consideration and in view of Applicant's arguments.

Claim Rejections - 35 USC § 102—new

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for

Art Unit: 1635

patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 32, 40, and 42 are rejected under 35 U.S.C. 102(e) as being anticipated by Tuschl et al. (WO 03/029459) "MicroRNA molecules."

Tuschl et al. disclosed the 22-nucleotide sequence of the mature mouse miR-151 (see Table 3, page 33; reproduced in part below). The sequence is 90% identical to instant SEQ ID NO:15, also 22-nucleotides in length, differing by only two nucleotides (underlined) from the mouse miR-151 disclosed by Tuschl et al.

20	miR-151	CUAGACUGA <u>AGCUCUUGAGGU</u>
		(SEQ ID NO:179)

Instant SEQ ID NO:15: cuagacugaagcuccuugagga

Tuschl et al. taught that mature miRNAs have a length of 19-24 nucleotides, but in particular are 21, 22, or 23 nucleotides long (pg. 3). Tuschl et al. further taught and claimed any nucleotide sequence identical or complementary to any of the sequences disclosed in Table 3 such as mouse miR-151, SEQ ID NO:179, including any sequence at least 80%, 90%, 95%, or 99% identical to the disclosed miRNA or its complement (pages 2 and 43). The sequences may be RNA or DNA (page 3). Accordingly, Tuschl et al. expressly contemplated (and therefore disclosed) every 22-nucleotide nucleic acid sequence that is 90% identical and complementary to the miR-151 disclosed therein at Table 3, shown above, including every DNA sequence encoding each possible 22-nucleotide sequence in this genus (see page 2 for example). At pages 4-5, Tuschl et al. taught vectors comprising these sequences. At page 21 it is taught that miRNAs are highly conserved and that almost every miRNA cloned from mouse was also encoded in the

human genome. Tuschl et al. expressly recommend cloning, sequencing, and detecting miRNAs in vertebrate and invertebrates using known techniques and those disclosed therein to investigate miRNA function.

In view of this disclosure, one of skill would instantly recognize each 22-nucleotide sequence 80% and 90% identical or complementary to the mouse miR-151 shown in Table 3 as fully as if each sequence was written out. This list of sequences necessarily includes instant SEQ ID NO:15 and its complements as well as DNA sequences encoding SEQ ID NO:15. These sequences are also indistinguishable from the instantly claimed probes.

Thus, Tuschl et al. anticipates the claimed nucleic acids.

Claims 39-42 are rejected under 35 U.S.C. 102(e) as being anticipated by Venter et al. (US Patent 6,812,339).

As amended on 5/15/2009, the claims read on vectors and probes comprising the “heterologous” sequences SEQ ID NO:15 and 6527. The claims do not exclude additional, unrecited “heterologous” sequences, adjacent to or contiguous with SEQ ID NO:15 and 6527 (MPEP 2111.03; *The transitional term "comprising" is inclusive or open-ended and does not exclude additional, unrecited elements or method steps*).

As shown by the alignment below, Venter et al. taught an SNP-containing nucleic acid sequence comprising instant SEQ ID NO:6527 and 15. Venter et al. further taught DNA and RNA vectors containing the SNP-containing nucleic acid (column 19, beginning at line 40, and elsewhere throughout the patent). The vectors disclosed by Venter et al. are indistinguishable

Art Unit: 1635

from the probes (i.e., nucleic acid) defined by claims 41 and 42 and would be capable of being used as a probe. Accordingly, the prior art disclosed the instantly claimed vectors and probes.

```
RESULT 1
US-09-949-016-13165
; Sequence 13165, Application US/09949016
; Patent No. 6812339
; GENERAL INFORMATION:
; APPLICANT: VENTER, J. Craig et al.
; TITLE OF INVENTION: POLYMORPHISMS IN KNOWN GENES ASSOCIATED
; TITLE OF INVENTION: WITH HUMAN DISEASE, METHODS OF DETECTION AND USES THEREOF
; FILE REFERENCE: CL001307
; CURRENT APPLICATION NUMBER: US/09/949,016
; CURRENT FILING DATE: 2000-04-14
; PRIOR APPLICATION NUMBER: 60/241,755
; PRIOR FILING DATE: 2000-10-20
; PRIOR APPLICATION NUMBER: 60/237,768
; PRIOR FILING DATE: 2000-10-03
; PRIOR APPLICATION NUMBER: 60/231,498
; PRIOR FILING DATE: 2000-09-08
; NUMBER OF SEQ ID NOS: 207012
; SOFTWARE: FastSEQ for Windows Version 4.0
; SEQ ID NO 13165
; LENGTH: 346112
; TYPE: DNA
; ORGANISM: Human
; FEATURE:
; NAME/KEY: misc_feature
; LOCATION: (1)...(346112)
; OTHER INFORMATION: n = A,T,C or G
US-09-949-016-13165
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```
Query Match          100.0%; Score 131; DB 3; Length 346112;
Best Local Similarity 74.8%; Pred. No. 6.3e-38;
Matches 98; Conservative 33; Mismatches 0; Indels 0; Gaps 0;
```

```
Qy      1  GCUAGUCACUGGGGCAAAGAUGACUAAAACACUUUCCUGCCUCGAGGAGCUCACAGUC 60
      ||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||
Db      270570 GCTAGTCACTGGGGCAAAGATGACTAAACACTTTTCCTGCCCTCGAGGAGCTCAGTC 270629

Qy      61  UAGUAUGUCUCAUCCCCUACUAGACUGAAGCCUCCUUGAGGACAGGGAUGGUCAUACUCAC 120
      :||::||::||::||::||::||::||::||::||::||::||::||::||::||::||
Db      270630 TAGTATGTCTCATCCCTACTAGACTGAAGCTCCTTGAGGACAGGGATGGTCATACTCAC 270689

Qy      121 CUCGGUGUUGC 131
      |::||::||::||
Db      270690 CTCGGTGTTC 270700
```

Claims 40 and 42 are rejected under 35 U.S.C. 102(b) as being anticipated by Zhao et al. (1997) GenBank Acc. No. AQ420078, first seen at NCBI on Mar 23 1999 12:30 AM.

As shown by the alignment below, Zhao et al. taught an isolated 684-nucleotide DNA sequence and BAC clone thereof comprising a sequence complementary to instant SEQ ID NO: 15. The vector disclosed by Zhao et al. is indistinguishable from the probe (i.e., nucleic acid)

Page 9

Page 9

Page 9

Lagos-Quintana et al. (2002) *Curr. Biol.* 12:735-739 taught a 22-nucleotide mouse miRNA, disclosed therein as miR-151, closely related and structurally similar to instant SEQ ID NO:15. See alignment below.

```
RESULT 16
MMU459763
LOCUS      MMU459763                22 bp      mRNA      linear      ROD 05-JUL-2002
DEFINITION Mus musculus microRNA miR-151.
ACCESSION  AJ459763
VERSION     AJ459763.1  GI:20799081
KEYWORDS    microRNA miR-151; miR-151 gene; miRNA.
SOURCE      Mus musculus (house mouse)
ORGANISM    Mus musculus
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
            Mammalia; Eutheria; Euarchontoglires; Glires; Rodentia;
            Sciurognathi; Muroidea; Muridae; Murinae; Mus.
REFERENCE   1
AUTHORS     Lagos-Quintana,M., Rauhut,R., Yalcin,A., Meyer,J., Lendeckel,W. and
            Tuschl,T.
TITLE       Identification of tissue-specific microRNAs from mouse
JOURNAL     Curr. Biol. 12 (9), 735-739 (2002)
PUBMED      12007417
REFERENCE   2  (bases 1 to 22)
AUTHORS     Tuschl,T.
TITLE       Direct Submission
JOURNAL     Submitted (06-MAY-2002) Dep. of Cellular Biochemistry, Max Planck
            Institute for Biophysical Chemistry, Am Fassberg 11, Goettingen
            37077, Germany
COMMENT     related sequence: TI88456669 (Trace Archive).
FEATURES
            Location/Qualifiers
            source                1. .22
                                   /organism="Mus musculus"
                                   /mol_type="mRNA"
                                   /db_xref="taxon:10090"
            gene                  1. .22
                                   /gene="miR-151"
            misc_RNA              1. .22
                                   /gene="miR-151"
                                   /product="microRNA miR-151"
                                   /note="transcribed as larger precursor, predicted to form
                                   hairpin"
ORIGIN
Query Match      14.8%;  Score 19.4;  DB 6;  Length 22;
Score over Length 88.2%;
Best Local Similarity 71.4%;  Pred. No. 9.8e+04;
Matches 15;  Conservative 5;  Mismatches 1;  Indels 0;  Gaps 0;

Qy      80 CUAGACUGAAGCUCCUUGAGG 100
        |:||||:| ||:||:||||
Db      1 CTAGACTGAGGCTCCTTGAGG 21
```

Conclusion

Claim 31 is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Louis Wollenberger whose telephone number is (571)272-8144. The examiner can normally be reached on M-F, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James (Doug) Schultz can be reached on (571)272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Louis Wollenberger/
Primary Examiner, Art Unit 1635
August 3, 2009

/JD Schultz/
Supervisory Patent Examiner, Art Unit 1635